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EXAMINER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/509,180	EISENBACH-SCHWARTZ ET AL.	
	Examiner	Art Unit	
	Kevin K. Hill, Ph.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30-42* is/are pending in the application.

4a) Of the above claim(s) *34,35,37,40 and 41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30-33,36,38,39 and 42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

1. Applicant's response to the Requirement for Restriction, filed on July 17, 2007 is acknowledged.

Applicant has elected the invention of Group II, Claims 30-42, drawn to a method for treating a disease which is susceptible to a T-cell- mediated autoimmune disease, wherein said method comprises the use of a pathogenic self- antigen, a peptide of said antigen, or a modified peptide of said antigen.

Within Group II, Applicant has elected the non-autoimmune species "glaucoma", and the antigen species "peptide of SEQ ID NO:5".

2. Election of Applicant's invention(s) was made with traverse.

Applicant argues that the "What all of the groups have in common, and what defines them all over the prior art, is the concept that T- cells activated by a pathogenic self-antigen associated with a T-cell mediated specific autoimmune disease of the organ being treated, cause amelioration of the non-autoimmune disease, disorder or injury being treated."

Applicants' arguments have been fully considered but are not found persuasive. MPEP §803 states that "If the search and examination of all the claims in an application can be made without serious burden, the examiner must examine them on the merits, even though they include claims to independent or distinct inventions."

In the instant case a serious burden exists since each limitation, directed to a structurally distinct amino acid sequence having a distinctly different physiological property from the other amino acid sequences, requires a separate, divergent, and non co-extensive search and examination of the patent and non-patent literature. For instance, a search and consideration of the prior art as it relates to SEQ ID NO:5 would not be adequate to uncover prior art related to SEQ ID NO:14.

Further, a search and examination of all the claims directed to all peptide embodiments involves different considerations of novelty, obviousness, written description, and enablement for each claim. The specification discloses that it is important to emphasize that the protection is

antigen-specific (pg 14, lines 3-4). The protection of one type of injury with one peptide will not necessarily be true for another peptide having activity for a different type of injury (pg 14, lines 5-6). Thus, the activity of one particular peptide for therapeutic treatment of one particular disease, disorder or injury will not necessarily anticipate a distinctly different peptide for therapeutic treatment of a different disease, disorder or injury. In view of these requirements, it is the Examiner's position that searching and examining all of the claims including all SEQ ID NO limitations in the same application presents a serious burden on the Examiner for the reasons given above and in the previous Restriction Requirement.

The requirement is still deemed proper and is therefore made FINAL.

Amendments

In the reply filed May 1, 2007, Applicant has withdrawn Claims 34-35, 37-38 and 40-41, and amended Claims 30-38 and 40-42.

3. Claims 34-35, 37 and 40-41 are pending but withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a non-elected invention, there being no allowable generic or linking claim.

4. Claims 30-33, 36, 38-39 and 42 are under consideration.

Priority

5. This application is a 371 of PCT/IL03/00251, filed March 25, 2003. Applicant's claim for the benefit of a prior-filed application parent provisional application 60/367,271, filed on March 26, 2002 under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged.

The disclosure of the prior-filed application, 60/367,271, filed on March 26, 2002, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application, specifically the peptide TSSEAATE (SEQ

ID NO:5) of claim 38. Support for the peptide TSSEAATE (SEQ ID NO:5) of claim 38 is found in PCT/IL03/00251, filed March 25, 2003.

Accordingly, the effective priority date of claim 38 is granted as March 25, 2003. If applicant believes the earlier applications provide support for this disclosure, applicant should point out such support by page and line number in the reply to this Action.

The effective priority date of claims 30-33, 36, 39 and 42 is granted as March 26, 2002.

Information Disclosure Statement

Applicant has filed an Information Disclosure Statement on September 27, 2004 that has been considered. The signed and initialed PTO Form 1449 is mailed with this action.

The listing of references in the specification (pgs 25-27) is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. **Claims 30-33, 36, 38-39 and 42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.** The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claimed invention is directed to a method of treating a disease, disorder or injury, the method comprising the immunization of an individual with an antigen. At issue for the purpose of written description requirements is the lack of support for the genus of immunogenic peptides that possess the claimed functional property(ies) that are pathogenic, and pathologically and immunologically protective upon vaccination for use in the claimed method to treat an enormous genus of etiologically and pathologically distinct diseases, disorders and injuries.

> *Vas-cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states that Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not clearly allow persons of ordinary skill in the art to recognize that (he or she) invented what is claimed." (See *Vas-cath* at page 1116).

> The disclosure of a single species is rarely, if ever, sufficient to describe a broad genus, particularly when the specification fails to describe the features of that genus, even in passing. (see *In re Shokal* 113USPQ283(CCPA1957); *Purdue Pharma L.P. vs Faulding Inc.* 56 USPQ2nd 1481 (CAFC 2000).

In analyzing whether the written description requirement is met for genus claims, it is first determined whether a representative number of species have been described by their complete structure. In the instant case, the peptide TSSEAATE (SEQ ID NO:5) is the only species whose complete structure is disclosed to be immunogenic. While the claims require the peptide to be a pathogenic self-antigen (claims 30(a), 32-33 and 36), the examiner notes that the instantly elected peptide embodiment TSSEAATE (SEQ ID NO:5) is considered by the art to be non-pathogenic (Singh et al, J. Immunology 152: 4699-4705, 1994).

Next, then, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics (i.e. other than nucleotide sequence), specific features and functional attributes that would distinguish different members of the claimed genus. The specification and claim(s) do not place any limit on the number of amino acid substitutions, deletions, insertions and/or additions that may be made to SEQ ID NO:5, or any peptide. Thus, the scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification does not disclose any amino acid substitution, deletion or insertion to demonstrate which amino acid sequence(s) is necessary for the required function in the claimed method. For example, while the specification discloses a preferred embodiment of the invention to consist in the use of peptides that are immunogenic, but not immunopathogenic (pg 12, lines 2-24), the specification does not disclose what amino acid sequences are necessary to distinguish pathogenic from non-pathogenic properties. The specification discloses that "[I]t is important to emphasize that the protection is antigen-specific." (pg 14, lines 3-4). Furthermore, the claims require the peptide to be protective upon vaccination to an enormous genus of etiologically and pathologically distinct diseases, disorders and injuries. However, no alteration is made to the SEQ ID NO:5 peptide or any peptide so as to demonstrate which amino acid(s) is necessary to retain immunogenicity, pathogenicity or non-pathogenicity, or provide pathological and immunological protection for use in the claimed method. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, SEQ ID NO:5 alone is insufficient to describe the genus.

The Revised Interim Guidelines state:

"The claimed invention as a whole may not be adequately described if the claims require an essential or critical element which is not adequately described in the specification and which is not conventional in the art" (col. 3, page 71434), "when there is substantial

variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus", "in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus" (col. 2, page 71436).

An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997).

Possession may also be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention. See, e.g., *Pfaff v. Wells Elecs., Inc.*, 525 U.S. 55, 68, 1 19 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998), *Regents of the University of California v. Eli Lilly*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997)*, *Amgen, Inc. v. Chugai Pharmaceutical*, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991) (one must define a compound by "whatever characteristics sufficiently distinguish it").

Therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. See *Fiers v. Revel*, 25 USPQ2d 1602 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. *In Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

> Without a correlation between structure and function, the claim does little more than define the claimed invention by function. That is not sufficient to satisfy the written description requirement. *See Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406 ("definition by function ... does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is").

Accordingly, given that the specification does not teach a correlation between structure and function of the exceptionally broadly-defined genus of immunogenic peptide antigens, this limited information is not deemed sufficient to reasonably convey to one skilled in the art that the applicant is in possession of the required starting materials to perform the necessary active steps and effect the claimed method, at the time the application was filed.

Thus, for the reasons outlined above, it is concluded that the claims do not meet the requirements for written description under 35 U.S.C. 112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

7. **Claims 30-33, 36, 38-39 and 42 are rejected under 35 U.S.C. 112, first paragraph**, because the specification, while being enabling for a method for protecting retinal ganglion cells from secondary degeneration and death induced as a consequence of axonal injury or glutamate toxicity in Fisher rats, the method comprising the administration of an immunogenic peptide consisting of the amino acid sequence TSSEAATE (SEQ ID NO:5), does not reasonably provide enablement for methods of treating an enormous genus of etiologically and pathologically distinct diseases, disorders or injuries in an enormous genus of physiologically distinct organs susceptible to T-cell-mediated specific autoimmune disease, the methods comprising the administration of an enormous genus of structurally undisclosed peptide antigens so as to block the T-cell response of immunopathogenic self-antigens. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

While determining whether a specification is enabling, one considers whether the claimed invention provides sufficient guidance to make and use the claimed invention. If not, whether an artisan would have required undue experimentation to make and use the claimed invention and whether working examples have been provided. When determining whether a specification meets the enablement requirements, some of the factors that need to be analyzed are: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and whether the quantity of any necessary experimentation to make or use the invention based on the content of the disclosure is "undue" (*In re Wands*, 858 F.2d 731, 737, 8 USPQ2ds 1400, 1404 (Fed. Cir. 1988)). Furthermore, USPTO does not have laboratory facilities to test if an invention will function as claimed when working examples are not disclosed in the specification. Therefore, enablement issues are raised and discussed based on the state of knowledge pertinent to an art at the time of the invention. And thus, skepticism raised in the enablement rejections are those raised in the art by artisans of expertise.

The Breadth of the Claims and The Nature of the Invention

With respect to the treatment method, the claims are broad for encompassing an enormous genus of etiologically and pathologically distinct diseases, disorders or injuries that may occur to an organ susceptible to a T-cell-mediated specific autoimmune disease. The art teaches, for example, that organ-specific autoimmune diseases affect a multitude of tissues and organs in the body, including the brain, retina, peripheral nerve, muscle, breast, and ovary, such as embrace multiple sclerosis, encephalomyelitis, neuritis, carditis, glomuleronephritis, otologic diseases that occur in association with a wide variety of systemic autoimmune and immunologic disorders: systemic lupus erythematosus, rheumatoid arthritis, Behçet's disease, Sjögren's syndrome, relapsing polychondritis, ulcerative colitis, Cogan's syndrome, and vasculitis-related disease, and insulin-dependent diabetes mellitus, autoimmune uveitis, rheumatoid arthritis, Addison's disease, thyroiditis, atrophic gastritis, myasthenia gravis, idiopathic thrombocytopenic purpura, hemolytic anemia, systemic lupus erythematosus, primary billary cirrhosis, Wegener's granulomatosis, polyarteritis nodosa, and inflammatory bowel disease.

With respect to the pathogenic self-antigen or peptide, the claims are broad for encompassing an enormous genus of structurally distinct peptides that lack a common structure or function. The claims place no limit in the number of amino acid residues that may be replaced, so long as the peptide retains the ability to be recognized by the T cell receptor.

The inventive concept in the instant application is that immune neuroprotective therapy is based on active T cell anti-self response which is insufficiently effective in its spontaneous form and is therefore in need of boosting (pg 15, lines 22-24). The use of analogs of peptides, in particular SEQ ID NO:5, derived from pathogenic antigens that are immunogenic, but not immunopathogenic, may be useful in the treatment of eye-specific injury, disorder or disease.

The Existence of Working Examples and The Amount of Direction Provided by the Inventor

The claims are drawn to a method of treating a disease, disorder or injury, wherein said disease, disorder or injury is other than an autoimmune disease. The specification discloses experimental methods of injuring the optic nerve or eye (pg 18, lines 1-17) and spinal cord contusion (pg 20, lines 4-9). However, the art recognizes (Schori et al, pg 3398, col. 1, Topic sentence; *of record in IDS) and the specification discloses (pg 23, lines 1-2) that optic nerve injury crush activates an autoimmune response. Thus, the specification does not disclose a working example by which a peptide treats a **non**-autoimmune disease, disorder or injury, nor does the specification provide a nexus between those injury models evoking an autoimmune response within which the inventive peptides are assayed, and those diseases, disorders or injuries that **do not** fundamentally and mechanistically evoke an autoimmune response as required by the claims.

The claims are drawn to an immunopathogenic peptide for use in the claimed method, wherein the instantly elected peptide embodiment is SEQ ID NO:5. The specification discloses that SEQ ID NO:5 demonstrates a degree of protection in Fisher rats against retinal ganglion cell loss as a consequence of injury (pg 23, Example 3). The examiner notes that the instantly elected peptide embodiment TSSEAATE (SEQ ID NO:5) is considered to be non-pathogenic (Singh et al, J. Immunology 152: 4699-4705, 1994), and thus is not a pathogenic self-antigen as required by the limitations of claims 30(a), 32-33 and 36. Furthermore, Figure 4 shows that the immunogenic peptide SEQ ID NO:5 works in Fisher rats, but not Lewis rats. Thus, a given

peptide does not work for all genetic backgrounds of individuals within a given species. The specification does not provide a nexus between genetic background of Fisher rats and enormous genetic background diversity extant in humans, nor an enabling means to identify a particular genetic background within a given organism within which the claimed immunogenic peptide will predictably function as opposed to those individuals who will experience no benefit. (See also pg 21, lines 23-24 for knowledge in the art that the genetic background influences the immunological and immunopathogenic response to a given peptide antigen.)

It is important to emphasize that the protection is antigen-specific (pg 14, lines 3-4). The protection of one type of injury with one peptide will not necessarily be true for another peptide having activity for a different type of injury (pg 14, lines 5-6). While the specification discloses a genus of contemplated sequences, with a preference for peptides that are immunogenic, but not immunopathogenic (pg 12, lines 22-24), it does not teach which amino acid(s) may be replaced in a given peptide so as to retain immunogenic, pathogenic or non-pathogenic properties, especially as applied to the enormous breadth of organ-specific diseases and disorders extant in the enormous genetic backgrounds of individuals embraced by the claims. The specification does not disclose how to identify those pathogenic peptides that are protective upon vaccination to an enormous genus of etiologically and pathologically distinct injuries and diseases.

The State of the Prior Art, The Level of One of Ordinary Skill and The Level of Predictability in the Art

The art teaches that autoimmunity as a benign physiological response, which, unless it gets out of control, reduces post-injury degeneration in the central nervous system (CNS) (Fisher et al, J. Neurosci. 21(1): 136-142, 2001; pg 141, col. 1, ¶2). The T cells that protect against CNS insults have the same phenotype as those implicated in the pathogenesis of autoimmune disease. The difference in their effects apparently lies in their regulation (Schwartz et al, Trends in Neuroscience 28(6): 297-302, 2003; * of record in IDS, pg 299, col. 1, ¶2). The optimal therapy should be based on immune modulation, not on immune suppression (Schwartz et al, IDS, pg 300, col. 1).

However, the complexity of the inflammatory response is reflected by the variables such as the nature of the damaged tissue, the stage of the inflammatory response, the animal species,

and the gender and genetic background of the individual (Schwartz et al, pg 298, col. 1, ¶3). The therapeutic window of the vaccination-induced neuroprotection will be determined by the choice of peptides and the route of administration. Immune activity in general, and autoimmune activity in particular, have been shown to have conflicting effects depending on the type of the immune cells, the timing, and the tissue context (Fisher et al, pg 141, col. 2, ¶1). It is difficult to estimate an appropriate dose for immunization of small peptide antigens because they may not have solid conformation and are always weaker antigens than that of the native polypeptide from which they are derived *in vivo* (Singh et al, J. Immunology 152: 4699-4705, 1994; pg 4700, col. 2, Results, ¶2).

With respect to the genus of peptides that are immunogenic, but not immunopathogenic, the art does not teach a means by which the artisan can predictably choose *a priori* a peptide derived from the amino acid sequence of a pathogenic self-antigen associated with a T-cell-mediated specific autoimmune disease for the genus of organs susceptible to a T-cell-mediated specific autoimmune disease. Typically, the artisan must first identify those peptides having immunopathogenic activity, and then modify the amino acid sequence of the immunopathogenic peptide to identify an immunogenic, but not immunopathogenic peptide antigen, as demonstrated by Singh et al, wherein the amino acid motif responsible for the immunopathogenic activity may consist of only three amino acids.

Thus, the art recognizes significant unpredictability in the ability to design an immunomodulatory peptide for the treatment of injury or disease, especially as the method is applied to an individual of unknown genetic background. Optimization for each specific peptide to the specific subject must be empirically determined for the specific disease or injury, the genetic background of the subject in need and the timing and dosing of the intended peptide so as to achieve a clinically meaningful result. In view of the breadth of the claimed immunogenic peptides, one of ordinary skill in the art would reasonably recognize significant unpredictability in identifying an amino acid sequence *a priori* that fulfills the therapeutic function of the claimed invention.

The Quantity of Any Necessary Experimentation to Make or Use the Invention

In the absence of specific guidance from the specification to identify those amino acids necessary for immunogenic activity while simultaneously blocking the immunopathogenic response of endogenous immunopathogenic peptides, the artisan is required to perform undue experimentation by trial and error to identify the desired peptide antigen for each of the etiologically and pathologically distinct diseases in the genus of physiologically distinct organs susceptible to a T-cell-mediated specific autoimmune disease. Furthermore, once having identified a potential therapeutic peptide, the artisan would then have to determine for themselves the necessary dose, timing and route of administration for an enormous genus of individuals having distinctly different genetic backgrounds, and thus distinctly different immunological responses to the immunogenic peptide, so as to achieve a clinically meaningful and therapeutic result. Thus, the quantity of necessary experimentation to make or use the invention as claimed, based upon what is known in the art and what has been disclosed in the specification, will create an undue burden for a person of ordinary skill in the art to demonstrate that the claimed genus of peptides may be used in the claimed therapeutic method.

As *In re Gardner, Roe and Willey*, 427 F.2d 786,789 (C.C.P.A. 1970), the skilled artisan might eventually find out how to use the invention after "a great deal of work". In the case of *In re Gardner, Roe and Willey*, the invention was a compound which the inventor claimed to have antidepressant activity, but was not enabled because the inventor failed to disclose how to use the invention based on insufficient disclosure of effective drug dosage. The court held that "the law requires that the disclosure in the application shall inform them how to use, not how to find out how to use for themselves". The specification does not provide the necessary correlation or nexus between the claimed immunogenic peptide consisting of the amino acid sequence TSSEAATE (SEQ ID NO:5) and its use protecting retinal ganglion cells from secondary degeneration and death induced as a consequence of axonal injury or glutamate toxicity in Fisher rats to the claimed enormous genus of structurally diverse peptides for the use in treating an enormous genus of etiologically and pathologically distinct diseases, disorders and injuries in an enormous genus of genetically diverse subjects.

The courts have stated that reasonable correlation must exist between scope of exclusive right to patent application and scope of enablement set forth in patent application. 27 USPQ2d

1662 *Exparte Maizel*. In the instant case, in view of the lack of guidance, working examples, breadth of the claims, the level of skill in the art and state of the art at the time of the claimed invention was made, it would have required undue experimentation to make and/or use the invention to the full scope as claimed.

In conclusion, the specification fails to provide any guidance as to how an artisan would have dealt with the art-recognized limitations of the claimed method commensurate with the scope of the claimed invention and therefore, limiting the claimed invention to a method for protecting retinal ganglion cells from secondary degeneration and death induced as a consequence of axonal injury or glutamate toxicity in Fisher rats, the method comprising the administration of an immunogenic peptide consisting of the amino acid sequence TSSEAATE (SEQ ID NO:5), is proper.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. **Claims 30-33, 36, 38-39 and 42 are rejected under 35 U.S.C. 112, second paragraph,** as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are vague in that no step(s) in the claimed method refers back to or recapitulates the preamble of claim 30. Applicant recites a method of treating a disease in an organ comprising the step of immunizing an individual, but no step is recited that actually accomplishes the preamble. It is unclear if additional, undisclosed steps are a part of the claimed method and therefore the metes and bounds of the claimed subject matter are unclear.

Claim 30 recites "said disease, disorder or injury is other than an autoimmune disease". It is unclear if the limitation "other than an autoimmune disease" is required only of "said disease" or is also required of "said... disorder or injury".

Claims 30(part c) and 36(part c) recite the limitation "the replacement" in reference to a modified peptide. There is insufficient antecedent basis for this limitation in the claim. No such specific replacement method step(s) is claimed prior to the use of the term "the replacement".

Claims 30(part c) and 36(part c) recite modified peptides having less affinity towards the T-cell receptor than the non-modified peptides, respectively. However, neither the claims nor the specification disclose the reference affinity value so as to apprise the artisan as to the metes and bounds of the claimed modified peptide.

Claim 31 recites the limitation "the eye" in reference to the organ of claim 30. There is insufficient antecedent basis for this limitation in the claim. No eye is claimed in claim 30.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. **Claims 30-32 and 39 are rejected under 35 U.S.C. 102(b)** as being anticipated by Kipnis et al (PNAS 97:97(13):7446-7451, 2000), as evidenced by Jiang et al (Cellular Immunol. 217:87-94, 2002).

Kipnis et al teach a method for treating crushed optic nerves that cause degeneration of the retinal ganglion cells in the eye, the method comprising the step of immunizing rats having the injury with the Cop-1 peptide (pg 7447, col. 2, Immunization).

With respect to the limitation that the peptide be a pathogenic self-antigen, peptide, or modified peptide thereof, associated with a T-cell-mediated specific autoimmune disease, the art recognizes that myelin basic protein (MBP) is a pathogenic self-antigen associated with acute idiopathic unilateral optic neuritis as well as acute relapses of the autoimmune disorder multiple sclerosis (Warren et al, J. Neurol. Sci. 109(1):88-95, 1992). The art also recognizes that MBP is a pathogenic self-antigen associated with autoimmune uveitis (Jiang et al). Thus, the Cop-1 peptide designed to mimic MBP fulfills the limitation of a modified peptide of a pathogenic self-antigen associated with a T-cell-mediated specific autoimmune disease.

10. **Claims 30-32 and 39 are rejected under 35 U.S.C. 102(b)** as being anticipated by Fisher et al (J. Neurosci. 21(1): 136-142, 2001).

Fisher et al teach a method for treating eye injury, specifically optic nerve injury (pg 137, col. 2, Crush) that cause degeneration of the retinal ganglion cells in the eye, the method comprising the step of administering a MOG peptide that is a self-antigen associated with a T-cell mediated specific autoimmune disease (pgs 136-137, joining ¶) to an individual having said injury (pg 139, Figure 4).

11. **Claims 30-32, 39 and 42 are rejected under 35 U.S.C. 102(b)** as being anticipated by Schori et al (PNAS 98(6):3398-3403, 2001; *of record in IDS), as evidenced by Jiang et al (Cellular Immunol. 217:87-94, 2002).

Schori et al teach a method for treating an injured optic nerve by intravitreal glutamate insult or crush injury that cause degeneration of the retinal ganglion cells in the eye or laser cauterization causing occlusion of the episcleral and limbal veins resulting in an increased intraocular pressure, the method comprising immunizing an individual, specifically a rat, with a peptide, Cop-1, the sequence of which is comprised within the sequence of a pathogenic self-antigen, specifically myelin basic protein (MBP), associated with a T-cell-mediated specific autoimmune disease such as autoimmune encephalomyelitis. Cop-1 is a synthetic peptide that cross-reacts with myelin antigen and is used clinically as an immunosuppressor of myelin-associated autoimmune disease, e.g. multiple sclerosis (pg 3398, col. 2, ¶1; pg 3401, col. 1, line 10). The art also recognizes that MBP is a pathogenic self-antigen associated with autoimmune uveitis (Jiang et al). Cop-1 can serve as an antagonist of the T cell antigen receptor for the immuno-dominant MBP epitope (pg 3402, col. 2, ¶3). Cop-1 provides highly effective protection from retinal ganglion cell (RGC) death induced by ocular hypertension in the rat model of glaucoma. Cop-1 is protective for optic nerve crush injury and ocular hypertension in rodents (pgs 3401-3402).

Conclusion

12. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kevin K. Hill, Ph.D. whose telephone number is 571-272-8036. The examiner can normally be reached on Monday through Friday, between 9:00am-6:00pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph T. Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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